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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SGAGIAS, MAGDALENE K	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,247	LU ET AL.	
	Examiner	Art Unit	
	Magdalene K. Sgagias	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *20-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending. Claims 1-19 are under consideration.

Applicant's election without traverse of Group I claims 1-19 in the reply filed on 12/01/06 is acknowledged.

Claims 20-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/01/06.

Claims 1-19 are under consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12, and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by **Gonczol et al,** (US 6,448,389 B1; 2002).

Gonczol et al, teaches a composition comprising a plurality of sets of nucleic acid molecules, encoding a different type of cytomegalovirus (CMV) polypeptide, and each molecule of a set encoding the same type of CMV polypeptide, wherein a plasmid pTet-gB, containing the portion of the HCMV genome (UL55) encoding gB. This plasmid further contains a tetracycline regulatable HCMV-immediate early promoter (column 1, lines 65-67, column 2,

lines 1-4). **Gonczol et al,** teaches a plasmid encoding the full-length gB subunit protein is a pΔRC-gB and another plasmid pΔRC-gB_{680}, containing the portion of the human CMV (HCMV) genome encoding the N-terminal 680 amino acids of the gB protein (column 2, lines 5-10). **Gonczol et al,** also teaches a pΔRC-pp65 plasmid which contains the portion of the HCMV genome (UL83) encoding the HCMV pp65 tegument protein and the pΔRC-pp150 plasmid which contains the portion of the HCMV genome (UL32) encoding the HCMV pp150 tegument protein (column 2, lines 10-15). **Gonczol et al,** further teaches of six mice inoculated with the pΔRC-pp65 alone at a single site, 3 mice responded with the pp65-specific lysis of target cells (figure 2) and in another experiment 3 of nine mice immunized with the pΔRC-pp65 alone showed strong pp65-sepcific CTL responses and CTL responses were also detected in 4 of 5 mice inoculated with a mixture of pΔRC-pp65 and pTet-gB. **Gonczol et al,** teaches a preparation of a pharmaceutically acceptable immunogenic composition, having appropriate pH, isotonicity, stability and other conventional characteristics, wherein the recombinant plasmid is suspended in isotonic water, phosphate buffered saline, or the like (wherein isotonic water and phosphate buffered saline read on a pharmaceutically acceptable carrier) (column 6, lines 30-40). When the pΔRC-pp65 and pTet-gB were inoculated separately into two different legs, 4 out 6 mice tested developed pp65-specifc CTL response (column 13, lines 14-25). These results establish that; 1) pp65-specifc CTL responses are induced after immunization; 2) there is no antigenic competition between gB and pp65 proteins in the induction of antibody and CTL responses; 3) gB protein expression in the cells at the inoculation site does no interfere with the presentation of pp65-specifc T cell epitopes by the MHC class I molecules (column 13, lines 20-25). Moreover, **Gonczol et al,** teaches pΔRC-gB_{680}, mixed with pΔRC-pp65 and given at one site or inoculated separately induce both gB- and pp65-specifc antibodies (column 16, example 13). **Gonczol et al,** provides DNA

molecules useful for in vitro and in vivo expression of antigenic fragments of the HCMV genome. Antigens include full-length and transmembrane-deleted fragments of gB such as gB.sub.1-680, pp65, pp150, and IE-exon-4. The DNA molecules of the invention are plasmids (column 3, lines 9-15). The inventors have found that these DNA molecules induce HCMV-specific immune responses, including ELISA and neutralizing antibodies and cytotoxic T lymphocytes (CTL), and are further useful in priming immune responses to subsequently administered HCMV immunogens and vaccines (columns 12-20, examples 9-14). As such **Gonczol et al,** anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gonczol et al,** (US 6,448,389 B1; 2002) in view of **Paoletti et al,** (US 6,267965, 2001).

Gonczol et al, teaches a composition comprising a plurality of sets of nucleic acid molecules, encoding a different type of cytomegalovirus (CMV) polypeptide, and each molecule of a set encoding the same type of CMV polypeptide, wherein a plasmid pTet-gB, containing the portion of the HCMV genome (UL55) encoding gB. This plasmid further contains a tetracycline regulatable HCMV-immediate early promoter (column 1, lines 65-67, column 2, lines 1-4). **Gonczol et al,** teaches a plasmid encoding the full-length gB subunit protein is a pΔRC-gB and another plasmid pΔRC-gB_{680}, containing the portion of the human CMV (HCMV) genome encoding the N-terminal 680 amino acids of the gB protein (column 2, lines 5-10). **Gonczol et**

al, also teaches a pΔRC-pp65 plasmid which contains the portion of the HCMV genome (UL83) encoding the HCMV pp65 tegument protein and the pΔRC-pp150 plasmid which contains the portion of the HCMV genome (UL32) encoding the HCMV pp150 tegument protein (column 2, lines 10-15). **Gonczol et al,** further teaches of six mice inoculated with the pΔRC-pp65 alone at a single site, 3 mice responded with the pp65-specific lysis of target cells (figure 2) and in another experiment 3 of nine mice immunized with the pΔRC-pp65 alone showed strong pp65-sepcific CTL responses and CTL responses were also detected in 4 of 5 mice inoculated with a mixture of pΔRC-pp65 and pTet-gB. **Gonczol et al,** teaches a preparation of a pharmaceutically acceptable immunogenic composition, having appropriate pH, isotonicity, stability and other conventional characteristics, wherein the recombinant plasmid is suspended in isotonic water, phosphate buffered saline, or the like (wherein isotonic water and phosphate buffered saline read on a pharmaceutically acceptable carrier) (column 6, lines 30-40). When the pΔRC-pp65 and pTet-gB were inoculated separately into two different legs, 4 out 6 mice tested developed pp65-specifc CTL response (column 13, lines 14-25). These results establish that; 1) pp65-specifc CTL responses are induced after immunization; 2) there is no antigenic competition between gB and pp65 proteins in the induction of antibody and CTL responses; 3) gB protein expression in the cells at the inoculation site does no interfere with the presentation of pp65-specifc T cell epitopes by the MHC class I molecules (column 13, lines 20-25). Moreover, **Gonczol et al,** teaches pΔRC-gB_{680}, mixed with pΔRC-pp65 and given at one site or inoculated separately induce both gB- and pp65-specifc antibodies (column 16, example 13). **Gonczol et al,** provides DNA molecules useful for in vitro and in vivo expression of antigenic fragments of the HCMV genome. Antigens include full-length and transmembrane-deleted fragments of gB such as gB.sub.1-680, pp65, pp150, and IE-exon-4. The DNA molecules of the invention are plasmids (column 3, lines 9-15). The inventors have found that these DNA molecules induce

HCMV-specific immune responses, including ELISA and neutralizing antibodies and cytotoxic T lymphocytes (CTL), and are further useful in priming immune responses to subsequently administered HCMV immunogens and vaccines (columns 12-20, examples 9-14). **Gonczol et al,** differs from the claimed invention by not teaching a composition wherein the polypeptides that induce the neutralizing antibody response comprise gcII or gcIII or their combinations or their antigenic fragments thereof.

However, at the time the claimed invention was made, **Paoletti et al,** teach HCMV is ubiquitous in humans, with usually mild or inapparent acute infection followed by persistence or latency. However, HCMV is a significant cause of morbidity and mortality in infants, most common infectious complication of organ transplantation in immunocompromised hosts, in AIDS patients, CMV retinitis is the leading cause of blindness [33]. Concerns remain about the use of a live HCMV vaccine because of the latency reactivation phenomenon characteristic of herpesvirus infections in humans and because of the capability of certain strains of HCMV to transform cells malignantly in vitro. For these reasons, a recombinant subunit CMV vaccine may be more acceptable for human immunization. **Paoletti et al**, teaches the role of individual HCMV proteins in protective immunity is unclear. Three immunologically distinct families of glycoproteins associated with the HCMV envelope have been described gCI (gp55 and gp93-130); gCII (gp47-52); and gCIII (gp85-pl45). Neutralization of HCMV has been demonstrated in vitro with antibodies specific for each of these glycoprotein families. The gene coding for gCI is homologous to HSV I gB. HCMVgB is synthesized as a glycosylated uncleaved precursor of apparent molecular weight 130-140 kDa which is processed by cellular proteinase into N-terminal 90-110 kDa and C-terminal 55-58 kDa products which remain associated in a disulfide linked complex. Monoclonal antibodies capable of neutralizing HCMV have been obtained from mice immunized with lysates of HCMV infected cells or HCMV virions, these monoclonals were

predominantly reactive with the C-terminal 55-58 kDa fragment. However, immunization with biochemically purified gP93 resulted in the development of gp93-specific neutralizing mAbs. Paoletti suggests it is an object of this invention to provide a method for expressing a gene product in a cell cultured in vitro using a modified recombinant virus or modified vector having an increased level of safety. As such, Paoletti et al provide sufficient motivation for one of ordinary skill in the art to apply the plasmid technology of Gonczol to induce the neutralizing antibody response comprise gcII or gcIII or their combinations or their antigenic fragments thereof for vaccine development.

Accordingly, in view of the teachings of Paoletti et al, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the palsmid technology of Gonczol by use of a gCii or gCII plasmid to induce the neutralizing antibody response comprise gcII or gcIII or their combinations or their antigenic fragments thereof in a mouse with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as it was an art-recognized goal to to provide a method to induce HCMV-specific immune responses, including neutralizing antibodies and cytotoxic T lymphocytes (CTL) for vaccines, by using a modified recombinant vector including each of these glycoprotein families (gcII-III) for an increased level of safety as taught by Gonczol et al, and particularly since Paoleti teaches neutralization of HCMV has been demonstrated with antibodies specific for each of these glycoprotein families (gcII-III) and moreover, since Gonczol et al suggest the role of individual HCMV proteins in protective immunity is unclear and HCMV is a significant cause of morbidity and mortality in infants, most common infectious complication of organ transplantation in immunocompromised hosts, in AIDS patients, CMV retinitis is the leading cause of blindness..

Thus, the claimed invention as a whole is clearly prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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